UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,704	05/16/2002	Camilo Anthony Leo Selwyn Colaco	8830-21	7595

7590 08/17/2010

Drinker Biddle & Reath
One Logan Square
18th & Cherry Streets
Philadelphia, PA 19103-6996

EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	PAPER NUMBER
1645	
MAIL DATE	DELIVERY MODE
08/17/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/049,704	COLACO, CAMILO ANTHONY LEO SELWYN	
	Examiner	Art Unit	
	GINNY PORTNER	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 17* is/are pending in the application.

4a) Of the above claim(s) *1-9, 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-14 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-15, and 17 are pending. Claims 10-14 and 17 are under consideration; claims 1-9, 15 stand withdrawn from consideration.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 18, 2010 has been entered.

Objections/Rejections Withdrawn

1. ***Withdrawn Double Patenting:*** Claims 10, 12 and 17 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, and 12 of copending Application No. 10/363,454 is herein withdrawn in light of the amendment of the claims to comprise a heat shock protein and a non-heat shock protein and claim 12 of the copending application has been canceled.

2. ***Withdrawn Objection*** Claim 13 objected to because of the informalities (typo) has been obviated by amending the claim to recite "comprises an aqueous carrier".

3. ***Withdrawn Objection*** The disclosure objected to because of the following informalities: At page 7 line 18 of the Specification, "Trypanosoma sp.." is described to be a bacteria, but is a parasite, not a bacteria has been obviated by deleting the term Trypanosoma sp..form the paragraph describing bacteria.

4. ***Withdrawn*** The rejection of claims 10-11 under 35 U.S.C. 102(b) as being anticipated by Wawrzynow et al (1995) is herein withdrawn in light of the fact that the λO protein is not described as being a subunit/fragment of a larger protein.

5. ***Withdrawn:***Claims 10, 11 and 13 rejected under 35 U.S.C. 102(b) as being anticipated by Laminet et al (EMBO Journal, 1990, vol. 9(7), pages 2315-139, in light of the amendment of the claims to comprise a heat shock protein and a non-heat shock protein

6.

Response to Arguments for Rejections Maintained

1. Applicant's arguments filed June 15, 2009 have been fully considered but they are not persuasive. ***Claim Rejections - 35 USC § 102***

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. ***Maintained***, The rejection of claims 10-11, 17 rejected under 35 U.S.C. 102(b) as being anticipated by Phipps et al (1991) in light of extrinsic evidence provided by Swiss-Prot Accession number O59663, is traversed on the grounds that the Figure 10 of Phipps et al shows a complex of two heat shock proteins of E.coli which has been excluded from the instant claims.

8. It is the position of the examiner that Phipps et al figure 10 is an immunoblot with antibodies directed to the ATPase and Heat shock protein complex, the antibodies being polyclonal in nature and would therefore contain antibodies to both the ATPase and the heat shock protein, the antibodies showing immunologically cross-reactivity with the E.coli ATPase/Heat Shock protein complex components shown in Figure 10. Phipps et al teach that one of the bands is an about 60 kd molecular weight protein (see page 171, col. 2, p. 2, middle of paragraph), and in light of Swiss-Prot accession number O59663 for Pyrodictium ATPase (see reference to Phipps et al cited in this record), the relative molecular weight for this ATPase is about 60 kd (572 amino acids).

Preparation of antiserum against the P.occultum complex
Antiserum was raised in a male rabbit by injection of a 1:1 (v/v) emulsion of the purified complex in Freund's complete adjuvant. Six injections of 20 µg protein each were administered subcutaneously in the back at intervals of one week, followed by a single intraperitoneal booster of 60 µg one week later. After another week, 35 ml of blood was taken from the large ear vein. Serum was stored at −20°C. Antibody specificity was determined by Ouchterlony double immunodiffusion in a gel consisting of 1% agarose in phosphate-buffered saline (Williams and Chase, 1971).

9.

10. Therefore the complex of Phipps et al comprises a heat shock protein complex formed through complexing with a peptide fragment of the whole ATPase with the active binding site of the heat shock protein, the ATPase being immunoreactive with antibodies directed to both the

Heat shock protein and the ATPase of the complex. Phipps et al still anticipates the instantly claimed invention as now claimed in light of the extrinsic evidence provided by Swiss-Prot Accession number O59663 which shows the ATPase to evidence a relative molecular weight of about 60 kD.

11. Phipps et al teach the isolation of the heat shock protein/peptide complexes produced by E.coli following heat shock (see page 1716, col. 2, last paragraph) based upon French press cell lysis/extracton ("Membrane-free French press lysates of several archae bacteria, the eubacteria E.coli (Also see page 1717, Figure 10, lane h. "Escherichia coli"; page 1717, col. 2, p. 2).

12. Traversal directed to increased constitutive expression, is being viewed by the examiner as being another way of saying induced higher levels of a constitutive protein (The E.coli complex was produced by heat shock which resulted in an induced/elevated synthesis of heat shock proteins: "The complex is preferentially accumulated following heat shock"; the "Living organisms including archaebacteria respond to an upshift in temperature by elevating the synthesis of a defined set of cellular proteins, known as heat shock proteins and accumulating them to higher steady state levels" (see page 1716, col. 2, last paragraph).

13. Traversal directed to inducible verses constitutive gene expression is not convincing because Applicant's Specification teaches the production of the claimed composition based upon constitutive expression in a genetically engineered bacteria without the need to apply external stresses (see Instant Specification page 7, p. 4), therefore Applicant's claims encompasses heat/stress protein/peptide complexes that may be produced by induction or constitutive expression, as long as the complex comprises the required products that include a heat shock protein complexed with a peptide and are endogenous to an extracellular pathogenic bacteria.

14. Phipps et al clearly teaches the induction of "A novel ATPase complex selectively accumulated upon heat shock (title)" and a similar process of induction (see page 1716, col. 2, last paragraph) was carried out with E.coli for evaluation of heat shock complexes based upon immunological cross-reactivity assay (see Figure 10, lane h); E.coli being a known human extracelluar pathogen.

15. No specific proteins of any specific relative molecular weight or structure are required by the instant claims, therefore the heat shock protein/peptide complex of E.coli contained in the composition obtained by and resulting in a membrane free French press lysate anticipates the instantly claimed invention as now claimed. The disclosure of Phipps et al still meets the requirements of the claims directed to compositions that comprise a heat shock protein/peptide complex produced by a heat shock stimulus, the complex is accomplished in an ATP dependent manner and is accomplished in an ATP-dependent reaction (see title "ATPase complex"; fig 9-10). The purification or production of a product by a particular process (i.e. the instant recombinant) does not impart novelty or unobviousness to a product when the product is taught by the prior art. This is particularly true, when the properties of the product are not changed by the process in an unexpected manner. *In re Thorpe*, 227 USPQ 964 (CAFC 1985); *In re Marosi*, 218 USPQ 289, 292-293 (CAFC 1983); and *In re Brown*, 173 USPQ 685 (CCPA 1972). Therefore, even if a particular process used to prepare a product is novel and unobvious over the prior art, the product *per se*, even when limited to the particular process, is unpatentable over the same product taught by the prior art. *In re King*, 107 F.2d 618, 620, 43 USPQ 400, 402 (CCPA 1939); *In re Merz*, 97 F.2d 559, 601, 38 USPQ 143-45 (CCPA 1938); and *United States v. Ciba-Geigy Corp.*, 508 F.supp. 1157, 1171, 211 USPQ 529, 543 (DNJ 1979).

1. Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594

16. The rejection of claims 10-14 and 17 rejected under 35 U.S.C. 102(b) as being anticipated by Ferrero et al (1995, reference of record.) in light of evidence provided by Schumann (2000) is traversed on the grounds that:

17. "urease is not an antigenic peptide fragment as required by the claims."

18. It is the position of the examiner that the Heat shock protein does not form a complex with the entire urease protein, but with an antigenic peptide fragment of an urease subunit, the claims reciting open language thus permitting the presence of additional amino acids in the complex of the heat shock protein complexes with a non-heat shock protein peptide fragment. The complexes of Ferrero et al comprise two molecules that contain peptide bonds, and the binding site between the two molecules are peptide fragments of the whole of each molecule; the complex of Ferrero et al comprising a heat shock protein of Helicobacter bound to a fragment peptide of a urease subunit.

19. Dunn et al (1990, Journal of Biological Chemistry) describes Helicobacter urease to be an about 380, 000 dalton enzyme (abstract, page 9464, col. 1, top half of paragraph) in crude extracts and an approximate 680,000 dalton molecule when purified (see page 9466, col. 1, bottom of first paragraph) but the subunits/fragments of Helicobacter urease are either 62 kDa or 30 kDa, and are therefore peptide fragments of the whole enzyme, the subunits of Helicobacter urease forming peptide complexes with a Helicobacter heat shock protein. The rejection of the claims is maintained for reasons of record and responses set forth herein above.

Ferrero et al disclose the instantly claimed invention directed to :
Instant claims 10-11, 17: composition that comprises a heat shock protein complex of HspA together with a peptide (urease (see page 6499, col. 2, p. 2 "The physical association between H. pylori HSP and urease") .

Claim 17 recites product by process language, but the composition of Ferrero et al is the same or equivalent product/composition produced by a different process The purification or production of a product by a particular process (i.e. heat shock process) does not impart novelty or unobviousness to a product when the product is taught by the prior art. This is particularly true, when the properties of the product are not changed by the process in an unexpected manner. *In re Thorpe*, 227 USPQ 964 (CAFC 1985); *In re Marosi*, 218 USPQ 289, 292-293 (CAFC 1983); and *In re Brown*, 173 USPQ 685 (CCPA 1972). Therefore, even if a particular process used to prepare a product is novel and unobvious over the prior art, the product *per se*, even when limited to the particular process, is unpatentable over the same product taught by the prior art. *In re King*, 107 F.2d 618, 620, 43 USPQ 400, 402 (CCPA 1939); *In re Merz*, 97 F.2d 559, 601, 38 USPQ 143-45 (CCPA 1938); and *United States v. Ciba-Geigy Corp.*, 508 F.supp. 1157, 1171, 211 USPQ 529, 543 (DNJ 1979).

Instant claim 12: the compositions further comprised an adjuvant

- Antigen extracts (50 ug of protein) containing 5 ug of cholera toxin" (a mucosal adjuvant)

Instant claim 13: together with an aqueous carrier ("were prepared in 0.1M sodium bicarbonate"(an aqueous carrier).

The heat shock proteins were expressed in situ and extracted from whole extracellular pathogenic bacteria (see page 6500, col. 1, Animal Experiments section H. felis).

Instant claim 14: Ferrero et al disclose a method of inducing an immune response in an animal ("mouse model") against infection by an extracellular pathogen (H. felis (mouse, cat and human pathogen) or H. pylori (mouse and human pathogen), the method comprising the step of:

Administering a pharmaceutically acceptable quantity (50 ug of antigen or 1 mg of whole cell sonicate, see Ledger for Table 2, page 6501) of a composition for inducing an immune response as claimed in claim 10 sufficient to elicit an immune response in the animal to said pathogenic bacteria (see Figure 2, page 6501, "serum antibodies" of HspA/UreB (whole cell extract/sonicate)) and Table 2, which shows 0/10 animal became infected).

Ferrero et al while not discussing the requirement for ATP in forming the HSP/peptide complex, but discloses the association of a Helicobacter heat shock protein and a peptide and therefore inherently anticipates the instantly claimed invention as now claimed, in light of evidence provided by Schumann that shows GroEL and GroES heat shock proteins to be ATP-dependent molecular chaperones (see Table 2, page 6) for associating with another peptide.

New Claim Limitations/New Grounds of Rejection

Claim Rejections - 35 USC § 112

20. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

21. Claims 10-14 and 17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 10-14 and 17 have been amended to recite the phrase "a non-heat shock protein derived endogenous" antigenic peptide fragment. Applicant points to page 6, line 1 and page 10, line 6.

22. The Specification at page 6 line 1 recites the following:

However, endogenous SP-complexes from extra-cellular procaryotic and protozoan pathogenic species, and more especially HSP-complexes from these organisms treated by heat shock or other stresses, have not been used as vaccines to immunise animals, notably vertebrates such as mammals, birds or fish against these infectious disease pathogens.

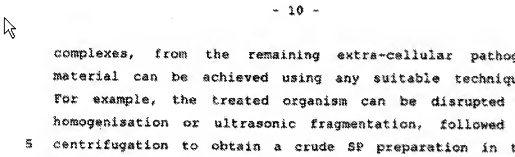
23. This narrative follows page 5 which discusses combinations of two heat shock proteins, to include HspA and HspB of Helicobacter pylori which form complexes together. The narrative at page 5 immediately before page 6 is as follows:

HSPs from extra-cellular pathogens themselves have also been utilised to immunise mammalian species as antigens *per se* but not as carriers of antigenic peptide fragments except as cojugates or hybrid fusion proteins. Thus WO 95/14093 discloses that the use of Helicobacter pylori HspA and B as immunogens elicits a good antibody response against these proteins and that this response is effective against the organism. Similarly, WO 96/40928 14093 discloses that the use of HSP 70 and 72 from Streptococcus elicits a good antibody response against these proteins and that this response is effective against the organism. Furthermore WO 90/02564 14093 discloses that the use of Trypanosomal, Mycoplasmal or Mycobacterial HSPs, and especially HSP70, as immunogens elicits a good antibody response against these proteins and that this should be effective against the respective organisms. Alternatively US 5830475 uses proteins expressed as fusions of the M.Bovis HSP genes as antigens and US 5736164 uses the T-cell epitope of hsp65 conjugated to poorly immunogenic antigens.

24.

25. The narrative at page 6, line 1 does not provide original descriptive support for the newly submitted negative claim limitation that excludes for the claims a complex derived from two heat shock proteins, in light of the fact that the narrative immediately following page 6 discusses combinations of two heat shock proteins that are known in the art to form heat shock protein complexes. No specific non-heat shock proteins are discussed or disclosed at page 6, line 1, or on the preceding page 5, lines 11-30 to which Applicant points as support the new combination of negative claim limitations.

26. Additionally Applicant points to page 10, line 6 in support for the newly submitted combination of claim limitations, the narrative from the instant Specification is shown as follows:



27. Line 6 of page 10 discusses "crude endogenous SP preparations", but this does not exclude the preparations that comprise a complex of two heat shock proteins.

The instant Specification does not provide original descriptive support for the exclusion of heat shock protein complexes that comprise two heat shock proteins based upon the narrative to which Applicant has pointed for original descriptive support for the newly submitted negative claim limitations recited in all claims under examination. The instant Specification does not

provide original descriptive support for excluding all heat shock protein complexes that comprise first and second heat shock proteins form the claims because the instant Specification specifically discusses combination complexes of two heat shock proteins at page 5 (narrative provided above) to be within the scope of the claims.

All of the claims under examination, claims 10-14 and 17, recite New Matter for reasons set forth above. Prior art rejections withdrawn based upon the newly submitted combination of claim limitations would be reinstated upon removal of the new matter.

Claim Rejections - 35 USC § 102

28. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

29. Claims 10-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Ding et al (1995, reference of record).

> Ding et al teach a Heat shock protein complex that forms in an ATP dependent manner, the complex being formed between a GroELS/5mer or 6-mer peptide fragment of a 42 kda head subunit protein of a bacteriophage, the complex forming endogenous complexes within E.coli. that were extracted/isolated from E.coli. Ding et al anticipates the instantly claimed invention as now claimed.

14922 *Biochemistry, Vol. 34, No. 45, 1995*

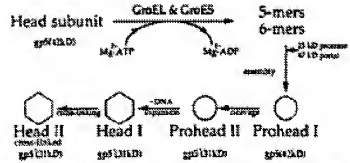


FIGURE 1: HK97 head assembly pathway (Duda et al., 1995a,b). The 42 kDa head subunit of HK97, gp5, folds and assembles into 5-mers and 6-mers with the assistance of the GroEL–Mg^{2+}–ATP system (Xie, 1994; Xie & Hendrix, 1995). The 5-mers and 6-mers, along with the viral protease and portal proteins assemble into prohead I. In the transition from prohead I to prohead II, each gp5 protein loses 102 amino acids from its N-terminus due to the action of the viral protease. DNA packaging triggers a conformational change of prohead II and causes its transition to head I. In head II, each of the major head subunits (gp5*) is covalently linked to its neighbors.

The purification or production of a product by a particular process (i.e. heat shock process) does not impart novelty or unobviousness to a product when the product is taught by the prior art. This is particularly true, when the properties of the product are not changed by the process in an unexpected manner. *In re Thorpe*, 227 USPQ 964 (CAFC 1985); *In re Marosi*, 218 USPQ 289, 292-293 (CAFC 1983); and *In re Brown*, 173 USPQ 685 (CCPA 1972). Therefore, even if a particular process used to prepare a product is novel and unobvious over the prior art, the product *per se*, even when limited to the particular process, is unpatentable over the same product taught by the prior art. *In re King*, 107 F.2d 618, 620, 43 USPQ 400, 402 (CCPA 1939); *In re Merz*, 97 F.2d 559, 601, 38 USPQ 143-45 (CCPA 1938); and *United States v. Ciba-Geigy Corp.*, 508 F.supp. 1157, 1171, 211 USPQ 529, 543 (DNJ 1979).

Conclusion

30. This is a non-final action.

31. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GINNY PORTNER whose telephone number is (571)272-0862. The examiner can normally be reached on flextime, but usually M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ginny Portner/
Examiner, Art Unit 1645
August 12, 2010

/Mark Navarro/

Primary Examiner, Art Unit 1645